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C. Rachal Winger
K&L Gates LLP
Suite 2900
925 Fourth Avenue
Seattle, WA 98104

EXAMINER	
SKIBINSKY, ANNA	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/707,576
Filing Date: November 06, 2000
Appellant(s): MAGNESS ET AL.

Jane E. Potter
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 8/18/2008 appealing from the Office action mailed 5/16/2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

This appeal involves claims 1-10, 14-26, 28, 31-44 and 46-55, which are rejected.

Claims 11-13, 27, 29-30 and 35 have been canceled.

Claims 56-61 are withdrawn.

(4) Status of Amendments After Final

One amendment after final has been filed, on 11/16/2007.

For purposes of clarification, the single after final amendment filed on November 16, 2007 was not entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection the o be reviewed on appeal is correct.

In view of the recent decision in *in re Bilski* (545 F.3d 943, 88 USPQ2d 1385 (Fed. Cir. 2008)), the rejection of claims 1-19, 47, 49, 50, and 51 under 35 USC 101 is hereby withdrawn.

Claims 1-10, 14-26, 28, 31-44 and 46-55 are rejected under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(**8) Evidence Relied Upon**

Ntais et al., "Meta-Analusis of the association of the Cathepsin D Ala224Val Gene Polymorphism with the Risk of Alzheimer's Disease: A HuGE Gene-Disease Association Review," American Journal of Epidemiology, vol. 159 (2004), pages 527-536.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10, 14-26, 28, 31-44 and 46-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Using data from the identified genetic variations of the ARU and ARA sub-populations to identify the drug target associated with a selected biological condition is not enabled.

3. In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must identify a drug target for an unspecified biological condition from data related to identified genetic variations for two subpopulations of subjects designated as “at risk affected” (ARA) and “at risk unaffected” (ARU) subpopulations. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The disclosure (see for example, page 25, line 19 through page 30, line 8) sets forth steps that are taken to analyze a population and define affected status, risk factors, and the characterization of the ARA, ARU, and URU phenotypes. The specification provides a working example of how to identify a gene associated with Hepatitis C. The claims however are directed to the identification of a drug target for "any" biological condition. The identification of a gene associated with hepatitis C. is not sufficient to enable the instant claims. The gene associated with hepatitis C is not an actual drug target for treatment of hepatitis C. Identification of a gene associated with Hepatitis C. does not enable the identification of a drug target. Furthermore, the disclosure does not provide any guidance as to what procedures or practices result in the identification of a **drug target** for "any" biological condition, as recited in the claims, using identified genetic variations between the ARA and ARU subpopulations.

c) The disclosure does not provide any examples wherein a drug target is identified. See above.

d) The nature of the invention, drug target identification, is complex.

e) The prior art teaches studies of e.g., hepatitis C, and it is acknowledged that the genetic basis for many specific diseases is known. However, even where the genetic basis of a disease is "known" or a genetic link to a disease has been identified, in many instances, the etiology of a disease is such that the "target" for treatment is not the gene itself. For example, it is well known in the art that the BRCA gene is used to identify those at risk of developing breast cancer however, the drug target for the disease is not the BRCA gene. The BRCA gene associated with the disease is known

but is not the target for drug treatment.

The prior art is silent in regards to methods or procedures wherein a drug target associated with an unspecified biological condition is identified through data related to genetic variations between ARA and ARU subpopulations, wherein no prior knowledge of a relationship between said target and said biological condition is available.

It is well known in the art how to define ARA and ARU populations and depending on the disease, it may be possible to find a genetic difference between two defined populations. However, as with the above cited example for breast cancer, the prior art does not teach that where a gene is known, the target for drug treatment is also known. The identification of a gene is not the same as identification of a drug target for the disease.

f) The skill of those in the art of drug target identification is high.

g) The unpredictability of identifying a drug target for an unspecified biological condition from data related to genetic variances is high, as the target for treatment (e.g. a drug) is not necessarily a gene, or a gene product, per se. For example, it is well known in the art that down- or up-regulation of expression of a protein (gene product) may cause a disorder or disease. Protein expression levels are controlled by a number of factors, including regulatory elements which bind to the gene itself, and inhibitors, activators, co-factors, etc. which control protein activity. This is supported by the instant specification, on page 11. Any of these factors may, in fact, be the "target" which needs to be addressed for appropriate treatment of the disease or disorder. Assuming one is, in fact, able to identify a gene product, and thus a (presumably) mutated gene

(variance) which is "involved" in a disease etiology, one can not then simply assume that the gene or its product is a "target" for treatment. Without further research to determine the actual causative element for the disease or disorder, or symptoms thereof, one would not know WHAT to target. If protein expression is down-regulated because the regulatory region of the gene is mutated such that transcriptional factors cannot bind appropriately, then the "target" can not be treated with a "drug;" one would have to actually alter the genetic sequence itself. It is noted that in this case, the disease itself may still be treated; perhaps by administration of higher levels of the protein; however, even if the protein were to be considered a "drug," the "drug" is not directed to a "target." Further, it is well known in the art that many diseases and disorders are not due to a single gene mutation (variance), but are the result of a constellation of reactions or interactions between several genes and/or gene products. One may identify a single mutated gene which is "involved" in a disease or disorder, but more research would be required to determine and/or confirm whether that gene (and mutation) are indeed causative for the disease or disorder symptoms before one can even begin to determine what an appropriate "target" for a drug would be. As it is well known that many factors may be involved in disease etiology, discovery of a mutated gene does not lead directly to identification of a drug target, but requires further experimentation. Thus, the degree of unpredictability for identifying a gene target is high.

h) The claims are broad in that they are drawn to identification of a drug target for an unspecified biological condition from data related to genetic variances, wherein the

genetic variances are not necessarily known to be correlated to a particular condition, and it is unknown whether any genetic variance found is actually a drug target for treatment of the unspecified condition.

The skilled practitioner would first turn to the instant disclosure for guidance in using the claimed invention. However, the disclosure lacks clear guidance for how to identify a drug target for an unspecified biological condition which is merely related to genetic variances, using only the claimed method steps. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not disclose methods or procedures for identifying a drug target for a given biological condition based on genetic variations between ARA and ARU subpopulations, wherein no prior knowledge of causative elements for the biological condition is available. Finally, due to the high level of unpredictability in the art set forth above, said practitioner would turn to trial and error experimentation to identify a drug target for a given biological condition using said data. Such amounts to undue experimentation.

For the reasons set forth above, the claims in the instant application to identifying the drug target associated with a selected biological condition are not enabled.

(10) Response to Argument

A. Summary of Appellant's Position

Appellants argue (Appeal Brief, page 14) that a person of skill in the art need only identify the biological manifestation of the genetic difference, such as an increase,

decrease, or a change in protein encoded by or regulated by the identified mutations to have the "drug target" associated with the ARU and ARA populations.

B. Appellant's Arguments

Appellants argue on page 3, section VI and page 11, of the Brief that the finality of the office action mailed May 16, 2007 is improper. It is noted that (a) the Office Action Summary clearly indicated finality and (b) this is a petitionable matter, therefore these arguments are moot with regard to this Appeal. Appellants further argue on pages 10 and 12 of the Brief that IF the after-final amendment of 12/20/2007 were entered, certain rejections would be overcome. This amendment was not entered for reasons of record therefore, these arguments are also moot.

With respect to Arguments, pages 12-13, directed as to whether the 35 USC 101 rejection is proper, it is noted that the 35 USC 101 rejection is withdrawn, therefore these arguments are moot.

With respect to Arguments, pages 4-6 of the Appeal Brief, Applicant's summarize the prosecution history.

With respect to Arguments on pages 7-9, Appellants summarize the Affidavits. The evidence presented in the Affidavits was addressed in detail in the Final Office Action filed 5/15/2007. As appellants merely summarize the evidence in the Affidavits, the summary is addressed herein. Further arguments with respect to enablement are set forth on page 14, paragraph 3 of the Appeal Brief.

Appellants argue (Brief, pages 6-7) that Dr. Cammie Lesser attests that it is routine to identify "at risk unaffected" (ARU) populations and that said expert testimony shows that the claims are enabled and to do require undue experimentation.

In response, Examiner agrees that it is routine to identify "at risk unaffected" (ARU) populations however, there are many genes that may be correlated with a phenotype/biological condition. In addition, any two populations which are not controlled for gender, race, etc. would be expected to have many genetic variations between them. Thus, while Dr. Lester's statement is correct, it is noted that the genetic differences identified between two populations, as recited in the claims, are not necessarily those associated with or causative of a disease, nor can they necessarily be used identify a drug target for the reasons set forth above.

Appellants argue (Brief, pages 7-8) that Dr. Richard Mayers attests that it would not require years to complete the identification of a drug target and it is possible and routine to identify a mutation without knowledge of the underlying disease mechanism.

In response, the examiner agrees that it is possible, and in fact has been routine for many years, to identify a mutation associated with a phenotype where no previous correlation between the mutation and the phenotype was previously known. If the correlation were previously known, such research would not be necessary. However, it is noted that in many cases, it is not possible to identify mutation(s) associated with a disease, nor specifically those which cause a disease. For example, despite many years of research, a mutation/variation has not yet been found which correlates to

Alzheimer's disease, or to multiple sclerosis. In these cases, it would be impossible to identify a drug target based on genetic variation between populations.

Appellants argue (Brief, page 8) that the affidavit of Dr. Iadonato attests that the first time the claimed methods were followed, they led to the discovery of a mutation that correlated with resistance to hepatitis C.

In response, it is noted that while a genetic variation was found which correlates to a specific disease, that genetic variation is not a drug target, but is merely a starting point for identifying a drug target. Thus, while it is admitted, as set forth above, that it is possible, and in fact has been routine for many years, to identify a mutation associated with a phenotype where no previous correlation between the mutation and the phenotype was previously known, it is maintained that in many cases, it is not possible to identify mutation(s) associated with a disease, nor specifically those which cause a disease.

Further, instant claim1 is not limited to a specific disease or a disorder. While instant claim 20 does recite a disease, it does not recite a specific disease, nor specifically Hepatitis C. It is further noted that the "at risk affected" (ARA) and "at risk unaffected" (ARU) populations of claim 1 are classified by phenotypic characteristic and not disease or disorder. Unlike the example of Hepatitis C set forth by Dr. Iadonato, the claimed populations are not limited to be those exposed to a virus. In fact, the instant claims are extremely broad and recite the identification of a drug target for any unspecified biological condition (e.g. claim 1) or disease (e.g. claim 20) from the identification of genetic differences between two populations. The claims are not limited

to the identification of a particular disease such as Hepatitis C nor are they directed to a method of drug discovery. It is further noted that the modified protein disclosed by Dr. Iadonoto is considered a drug, not a drug target as recited in the claims.

Appellants argue (Appeal Brief, page 14) that a person of skill in the art need only to identify the biological manifestation of the genetic difference, whether an increase or decrease or a change in protein encoded by or regulated by the identified mutations to have the "drug target" associated with the "at risk unaffected" (ARU) and "at risk affected" (ARA) populations.

In response, while the specification does provide guidance for how to develop a drug when a polypeptide is known to be the target (e.g. page 8 of the specification), the specification does not provide any guidance for how identify a drug target based only on identification of genetic variations between ARA and ARU (and sometimes URU) populations. Even where the claims recite a disease and genetic testing, as in claim 20, the specification does not teach, using only the method steps recited in the claims, how to determine whether any genetic variation found is indeed correlated to the disease, nor how to identify from the variation information only, what a "target" for a drug or drug treatment should be.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Anna Skibinsky, Ph.D.
Examiner
Art Unit 1631

/Lori A. Clow/
Primary Examiner, Art Unit 1631

Conferees:

Marjorie Moran

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631

Bennett Celsa

/Bennett Celsa/
Quality Assurance Specialist –TC 1600